

## Decreased Maternal Age With Hydranencephaly

Mark S. Lubinsky,<sup>1,2\*</sup> William Adkins,<sup>3</sup> and Elizabeth G. Kaveggia<sup>3</sup>

<sup>1</sup>Department of Pediatrics, Medical College of Wisconsin, Milwaukee

<sup>2</sup>Genetics Center, Children's Hospital of Wisconsin, Milwaukee

<sup>3</sup>Central Wisconsin Center for the Developmentally Disabled, Madison, Wisconsin

**We studied parental ages of institutionalized children with hydranencephaly. Mothers under age 20 years and under age 18 years were, respectively, 5 and 10 times as frequent as in the general population, and 3 and 4 times more frequent than for institutionalized control patients. Unwed mothers were also common, but may reflect high rates in younger mothers combined with institutionalization bias. Thus, hydranencephaly appears to show a decreased maternal age effect, similar to that seen with other conditions presumably due to prenatal vascular disruptions. Am. J. Med. Genet. 69: 232–234, 1997. © 1997 Wiley-Liss, Inc.**

**KEY WORDS:** hydranencephaly; maternal age; vascular disruption

### INTRODUCTION

Gastroschisis, which is caused by presumed prenatal vascular events, is associated with decreased maternal age [Torfs et al., 1994]. Since hydranencephaly (absent cerebral hemispheres) has an apparently similar pathogenesis [Hunter, 1993], and increased incidences with unwed (and, therefore, possibly younger) mothers [Opitz et al., 1978, 1982; Friede, 1989], we studied institutionalized children with this finding for evidence of a similar parental age effect.

### MATERIALS AND METHODS

The Central Wisconsin Center for the Developmentally Disabled (CWC) is a state institution for complete or intensive medical-nursing care of severely and profoundly retarded children under age 7 years. Cases were reviewed as part of an ongoing project coordinated with clinical care, details of which are reported elsewhere [Opitz et al., 1978, 1982].

This paper is dedicated, with much gratitude, to Dr. John M. Opitz in commemoration of his sixtieth birthday.

\*Correspondence to: Mark Lubinsky, M.D., Genetics Center, Children's Hospital of Wisconsin, P.O. Box 1997, Mail Station 716, Milwaukee, WI 53201.

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Fluid replacement of at least one cerebral hemisphere, with no more than a tissue rim remaining, was confirmed by autopsy or brain imaging, save for one case with total frontal transillumination, low frontal EEG amplitude, and a typical clinical picture. Cases with additional diagnoses or known postnatal causes were excluded.

We noted marital status, birth history, and race. Parental ages were by dates, save for one 17-year-old mother who was assigned an age of 17.50 years. Population controls used Wisconsin Department of Health and Human Services (DHSS) [1990] statistics for 1968–1988, and statistics courtesy of M. Soref, Ph.D., for 1963–1967, which were mostly by 2-year intervals for women age <20 years. We used averages of state values matched to birth years of each case (e.g., if two cases were born in 1978, the state value for 1978 was counted twice). CWC controls were 81 CWC cases with primary (nonsyndromic and nonchromosomal) central nervous system malformations. The most common diagnoses were spina bifida (36 cases), holoprosencephaly (12 cases), encephalocele (9 cases), and Arnold-Chiari (6 cases) and Dandy Walker malformations (5 cases).

### RESULTS

Births were from 1964–1985, with 14 bilateral and 2 unilateral cases. One child was black and 15 were white, and one had been born prematurely. Birth head circumference, when known, was >95th centile in 4 and normal in 3.

Average maternal age was 21.03 years. Ten mothers were <20 years old (62.5%), while the average population frequency of teenage mothers for corresponding birth years was 12.1%, for a roughly 5-fold excess ( $\chi^2 = 39.2$ ,  $P < 0.001$ ). Six mothers were <18 years old (37.5%), compared to an average population frequency of 3.6%, a roughly 10-fold excess ( $\chi^2 = 52.55$ ,  $P < 0.001$ ).

Of 9 unwed mothers, 8 (56.25%) were under age 19 years.

Average paternal age was 25.46 years, but data were absent for 7 cases with mothers age 21 years or younger (Table I). For CWC controls, maternal ages (Fig. 1 and Table II) averaged 26.7 years, with 7 mothers <18 years old (expected = 3), and 15 mothers <20 years old (expected = 8). Mothers <20 years old were 3-fold more

TABLE I. Parental Ages in Years\*

Mothers	Fathers
15.79 <sup>a</sup>	?
16.69 <sup>a</sup>	19.72
17.06	?
17.50 <sup>a</sup> (est)	?
17.50 <sup>a</sup>	?
17.61 <sup>a</sup>	?
18.02 <sup>a</sup>	?
18.50 <sup>a</sup>	19.15
18.61	21.69
18.86 <sup>a</sup>	?
20.71	?
21.97	26.36
25.03 <sup>a</sup>	22.68
27.84	27.70
28.59	32.26
36.28	34.11

\* est, estimated fractional age.

<sup>a</sup> Unwed mother.

frequent, and <18 years old 4-fold more frequent in the hydranencephalic group than with these controls, still highly significant (Table III).

### DISCUSSION

CWC patients with hydranencephaly had five times as many mothers <20 years old as did children in the general population, and 10 times as many mothers <18 years old. Institutionalization biases are likely, but compared to institutionalized controls, excesses were 3- and 4-fold, respectively; in fact, there were slightly fewer control mothers <19 years old (9 vs. 10) despite total numbers five times as great (81 vs. 16). Excesses were highly significant in all cases (Table III).

Unwed mothers were common, as noted by Lange-Cosack [Friede, 1989], and previously in CWC hydranencephaly cases [Opitz et al., 1978, 1982]. In our cases, almost all such births were to teenage mothers, 80% of whom were unwed, a finding generally

TABLE II. Percentages of Mothers &lt;20 and &lt;18 Years Old in the State of Wisconsin, Matched by Year With CWC Cases

Birth year, CWC cases	Maternal age, CWC cases	Population frequencies (%)	
		Mothers <20 years old	Mothers <18 years old
1964	28.59	9.1	2.3
1965	27.84	9.9	2.3
1967	17.50	11.6	2.7
1968	20.17	11.5	2.9
1969	18.61	12.2	3.2
1970	25.03	12.5	3.4
1971	17.61	13.1	3.7
1972	36.28	14.2	4.5
1973	18.50	15.6	5.0
1975	16.69	14.8	5.1
1978	15.79	12.9	4.3
1978	21.97	12.9	4.3
1981	17.06	11.8	3.7
1982	18.02	11.0	3.4
1985	18.86	10.2	3.6
1985	17.50	10.2	3.6
Average:		12.1	3.6

common in this group (e.g., 60% or more Wisconsin mothers <18 years old from 1975 [Guhleman, 1993]), especially in lower ages. While numbers are small and many biases are possible, an increase may still be real.

Ages of most partners of teenage mothers are missing, but for the rest, the average age of mothers was 24.18 years, and of fathers 25.46 years, supporting no great discrepancy between parental ages (Table I).

There was no excess of premature births or difficult deliveries to suggest postnatal events, and increased head sizes at birth show that at least some cases were of prenatal onset.

In our study hydranencephaly shows a decreased maternal age effect similar to that seen with gastroschisis, another apparent prenatal vascular disruption [Torfs et al., 1994]. A maternal age effect may therefore be generally associated with prenatal vascular events. However, the cause of this phenomenon is unknown.

### CONCLUSIONS

Institutionalized children with hydranencephaly have a significant excess of younger and deficit of older mothers, apparently unexplained by biases of ascertainment or as excess perinatal complications. This may be part of a general association of prenatal vascular disruptions and decreased maternal age, the cause of which is unknown. A relationship to unwed maternal status is possible, but uncertain.

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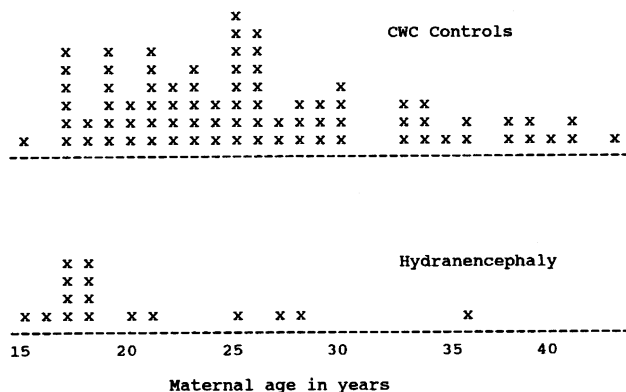


Fig. 1. Maternal age distributions.

TABLE III. Chi-Square Analysis

Observed and expected				
Case ages	<20 years	>20 years	<18 years	>18 years
Observed	10	6	6	10
Expected	1.9	14.1	0.58	15.42
(general)				
Expected	3	13	1.4	14.6
(control)				
Computations of chi-square (for one degree of freedom)				
	General population controls		CWC controls	
<20 years	$\frac{(1.9 - 10)^2}{1.9} + \frac{(14.1 - 6)^2}{14.1} = 39.18$		$\frac{(3 - 10)^2}{3} + \frac{(13 - 6)^2}{13} = 20.1$	
< 18 years	$\frac{(0.58 - 6)^2}{0.58} + \frac{(15.42 - 10)^2}{15.42} = 52.55$		$\frac{(1.4 - 6)^2}{1.4} + \frac{(14.6 - 10)^2}{14.6} = 15.11$	

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